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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/628,803	07/28/00	MURPHY J	112910.3302

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PEPPER HAMILTON LLP
GILBERTO M VILLACORTA PH D
600 FOURTHEENTH STREET NW
WASHINGTON DC 20005-2004

EXAMINER	
HUI, S	
ART UNIT	**PAPER NUMBER**
1617	10

DATE MAILED: 09/25/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/628,803	Applicant(s) MURPHY ET AL.	
	Examiner San-ming Hui	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 July 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20 and 33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment filed July 10, 2001, in Paper No. 9 is acknowledged and has been entered.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-20 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bourzat et al. (USPN 4,960,779 from the Information Disclosure Statement received March 14, 2001) and Doble et al. (J Pharmacol Exp Ther 266(3):1213-26 from the Information Disclosure Statement received March 14, 2001) in view of Novo Nordisk (English abstract of Denmark Patent DK9800727 from the Information Disclosure Statement received March 14, 2001) and Sandyk (Abstract from International Journal of Neuroscience, 1995, 83(1-2): 81-92; Medline, AN:96357641) references of record in the office action mailed April 10, 2001.

Bourzat et al. teaches a method of administering pyrrole compounds including pagoclone in a dose of 10 to 500mg daily (See claim 11 and 12; also col. 20, line 3-5 and 28-30). Bourzat et al. teaches that the routes of administration of the pyrrole compounds including pagoclone may be oral, rectal, parenteral, and percutaneous (See col. 19, lines 28-29).

Doble et al. teaches that pagoclone is a partial agonist of $GABA_A$ receptor (see page 1224, col.2, first paragraph and page 1225, first col., last paragraph).

However, the primary references do not expressly teach the administration of pagoclone in methods of treating stuttering. Also, the references do not expressly teach the dosage of pagoclone herein.

Novo Nordisk teaches that stuttering is a disorder which is related to GABA-uptake activity (See abstract).

Sandyk teaches that the immediate improvement of dysarthria stuttering is the result of changes in the synthesis and release of GABA.

Therefore it would have been obvious for one of ordinary skill in the art at the time the invention was made to administer pagoclone to a patient in a method to treat stuttering.

One of ordinary skill in the art would have been motivated to administer pagoclone in a method to treat stuttering because the release of GABA or the increase of GABA levels are known to be associated with dysarthria and stuttering in the prior art. Therefore administering to patients suffering from stuttering any known $GABA_A$ modulator including the elected compound, known to increase the GABA level, would be expected to produce beneficial effects in the treatment of a patient suffering from stuttering or dysarthria.

The optimization of result effect parameters (e.g., dosage range and dosage regimen) is obvious as being within the skill of the artisan.

Response to Remarks

Applicant's remarks submitted July 10, 2001 regarding the compounds of the present invention not being directly involved in the release or synthesis of GABA itself has been considered but found unpersuasive as to the non-obviousness of using pagoclone in a method of treating stuttering because pagoclone is known to be a partial $GABA_A$ agonist and therefore would be expected to, when binding to the GABA receptor, increase GABA neurotransmitter function. Based on Sandyk, the immediate improvement of stuttering was observed with increasing GABA neurotransmitter function. Therefore, one of ordinary skill in the art would reasonably expect any ligand having agonistic properties at the GABA receptor to bind to the GABA receptor, including an agonist (GABA itself) or a partial agonist (pagoclone), to increase GABA neurotransmitter function and be useful in improving or treating stuttering.

Applicant's remarks regarding the uptake of neurotransmitters from the synapses of neurons (as discussed in Novo Nordisk) involving a different biochemical pathway than neurotransmitter binding to receptors have been considered but found unpersuasive because of the reasons stated in the paragraph immediately above. One of ordinary skill in the art would have found it obvious to employ any GABA agonists or partial agonist including pagoclone to treat stuttering because based on Sandyk, increasing GABA neurotransmitter activity is known to improve stuttering. Pagoclone is known to be a partial GABA agonist and therefore it would be reasonably expected to have similar GABA receptor mediated effects and be useful to treat stuttering.

In regard to any possible unexpected result over the prior art from the method of using pagoclone to treat stuttering, examples 6.1, 6.2, and 6.4 (the only examples in the specification relating to the elected compound, pagoclone) have been considered but are not found persuasive because pagoclone would have been expected to be useful to treat stuttering based on the cited prior art. It is applicant's burden to demonstrate unexpected results over the prior art. See MPEP 716.02, also 716.02 (a) - (g). Furthermore, the unexpected results should be demonstrated with evidence that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance. *Ex parte Gelles*, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992). Moreover, evidence as to any unexpected benefits must be "clear and convincing" *In re Lohr*, 137 USPQ 548 (CCPA 1963), and be of a scope reasonably commensurate with the scope of the subject matter claimed, *In re Linder*, 173 USPQ 356 (CCPA 1972). In the instant case, example 6.1 demonstrates the improvement of stuttering when pagoclone is administered. This is seen to be an expected effect based on the cited prior art. No convincing and clear unexpected result is seen. For example 6.2 and 6.4, no result is presented for evaluation of a possible unexpected benefit.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Minna Moezie, J.D., can be reached on (703) 308-4612. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

San-ming Hui
September 24, 2001

MINNA MOEZIE, J.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600